Amendments to the Claims:

Prior to this amendment, claims 1-88 were pending.

Please cancel claims 2, 3, 17, 18, 20-26, 28, 31-42, and 48-71.

Please amend claims 1, 4-11, 13-16, 19, 27, 29, 30, 43-47, and 72-88.

Support for amended claims 1, 4-11, 13-16, 19, 27, 29, 30, 43-47, and 72-88 may be found in the original claims and specification as filed.

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method of inhibiting in a mammal formation of neutralizing antibodies directed against a heterologous protein, comprising:

co-administering to said mammal, an ~~agent~~ adenovirus in an amount sufficient to deplete or inhibit at least some antigen presenting cells of said mammal, and ~~a heterologous protein and/or~~ a nucleic acid sequence encoding said heterologous protein, said ~~agent~~ adenovirus being administered prior to or simultaneously with said ~~heterologous protein and/or~~ nucleic acid sequence, thereby inhibiting the production of neutralizing antibodies against said heterologous protein.

2. (Canceled)

3. (Canceled)

4. (Currently Amended) ~~Method~~ The method according to claim ~~3~~ 1, wherein said adenovirus is selected ~~among~~ from wild type human adenovirus ~~and~~, recombinant adenovirus, ~~or~~ and a fragment thereof.

5. (Currently Amended) ~~A~~ The method according to ~~any one of claims 1 to 4~~ claim 1 or 4, wherein said antigen presenting cells are antigen presenting cells located in the liver of said mammal.

6. (Currently Amended) ~~A~~ The method according to claim ~~2~~ 1, wherein said ~~agent~~ adenovirus is administered prior to said ~~heterologous protein and/or said~~ nucleic acid sequence encoding said heterologous protein.

7. (Currently Amended) ~~Method~~ The method according to claim ~~2~~ 1, wherein said ~~agent~~ adenovirus is administered simultaneously to ~~said heterologous protein and/or~~ said nucleic acid sequence encoding said heterologous protein.

8. (Currently Amended) ~~A~~ The method according to claim 7, wherein said ~~agent~~ adenovirus and said nucleic acid sequence encoding said heterologous protein are simultaneously co-administered as a recombinant ~~virus~~ adenovirus, the genome of which comprises at least one nucleic acid sequence encoding said heterologous protein.

9. (Currently Amended) ~~A~~ The method according to claim 8, wherein the genome of said recombinant ~~virus~~ adenovirus comprises at least regulatory sequences necessary to direct the expression of said heterologous protein in at least one antigen presenting cell of said mammal.

10. (Currently Amended) ~~A~~ The method according to claim 9, wherein said regulatory sequences ~~comprises~~ comprise promoter sequences selected from the group consisting of cytomegalovirus early promoter (CMV IEP), Rous sarcoma virus long terminal repeat promoter (RSV LTR), myeloproliferative sarcoma virus long terminal repeat (MPSV LTR), simian virus 40 early promoter (SV40 IEP), and major late promoter of the adenovirus.

11. (Currently Amended) ~~A~~ The method according to any one of claims ~~1 to 10~~ 1 and 4-10, further comprising administering to said mammal an ~~additional~~ agent to enhance the depletion and/or the inhibition of at least some antigen presenting cells of said mammal.

12. (Previously Presented) A method of inhibiting in a mammal formation of neutralizing antibodies directed against a heterologous protein comprising administering to said mammal a recombinant adenovirus, the genome of which comprises at least a nucleic acid sequence encoding said heterologous protein and regulatory sequences, in an amount sufficient to deplete or inhibit at least some antigen presenting cells of said mammal, thereby inhibiting the production of neutralizing antibodies against said heterologous protein.

13. (Currently Amended) ~~A~~ The method according to claim 12, further comprising administering to said mammal an additional adenovirus or a fragment thereof, the genome of which is not expressing said heterologous protein, thereby enhancing the amount of adenoviruses to deplete or inhibit at least some antigen presenting cells of said mammal.

14. (Currently Amended) ~~A~~ The method according to ~~any one of claims 12 to 13~~ claim 12 or 13, wherein said mammal is a mouse and wherein the amount of adenovirus ~~particules~~ particles administered to deplete or inhibit at least some antigen presenting cells of said mouse is equal to or greater ~~to~~ than about ~~4.10^{10}~~ 4×10^{10} particles, said particles comprising optionally said additional adenovirus.

15. (Currently Amended) ~~Method~~ The method according to claim 14, wherein the amount of adenovirus ~~particules~~ particles administered to deplete or ~~inhibits~~ inhibit at least some antigen presenting cells of said mouse is equal to or greater ~~to~~ than about ~~6.10^{10}~~ 6×10^{10} particles.

16. (Currently Amended) ~~A~~ The method according to ~~any one of claims 14 to 15~~ claim 14 or 15, wherein the amount of said recombinant adenovirus able to form ~~plaque~~ plaques, is equal to or greater ~~to~~ than about ~~4.10^{9}~~ 4×10^{9} pfu/mouse.

17-18. (Canceled)

19. (Currently Amended) A method for reducing an anti-heterologous protein immune response in a mammal, including human, subject to the administration of said ~~heterologous protein and/or~~ nucleic acid sequence encoding said heterologous protein, said method comprising inhibiting in said mammal the formation of neutralizing antibodies directed against said heterologous protein by the method according to any one of claims ~~1 to 16~~ 1 and 4-16.

20-26. (Canceled)

27. (Currently Amended) A method of inhibiting in a mammal formation of neutralizing antibodies directed against a heterologous protein, said method comprising:

(i) Optionally, co-administering to a first mammal, at least one ~~agent~~ adenovirus and ~~said heterologous protein and/or~~ a nucleic acid sequence encoding said heterologous protein, said ~~agent~~ adenovirus being administered simultaneously, sequentially or separately with said ~~heterologous protein and/or~~ nucleic acid sequence, and determining at least one amount of said heterologous protein and said ~~agent~~ adenovirus, sufficient to trigger an immune response against said heterologous protein by said first mammal; optionally, re-performing step (i) until said amount is determined;

(ii) co-administering to a second mammal said ~~heterologous protein and/or~~ nucleic acid sequence encoding said heterologous protein, in an amount sufficient to trigger an immune response against said heterologous protein, as determined at step (i) and prior to or simultaneously administering said ~~agent~~ adenovirus, in an amount greater that the one determined at step (i) and sufficient to trigger an immune response against said ~~agent~~ adenovirus and sufficient to deplete or inhibit at least some antigen presenting cells of said mammal, and determining for said second mammal at least one amount of said ~~agent~~ adenovirus that reduces and/or suppresses the anti-heterologous protein immune response in said mammal; and re-performing step (ii) until said amount is determined; ~~and~~ wherein ~~when one co-administers to said mammal~~ said ~~heterologous protein and/or~~ nucleic acid sequence encoding said heterologous protein is co-adminstered to said mammal, ~~and~~ prior to or simultaneously with an ~~agent~~ adenovirus in an amount equal to or greater than the one

determined at step (ii), and wherein said mammal produces neutralizing antibodies against said ~~agent~~ adenovirus but produces no or few neutralizing antibodies against said heterologous protein.

28. (Canceled)

29. (Currently Amended) A method for therapy of a mammal affected by a disease wherein at least one endogenous protein is involved in said disease etiology, said method comprising inhibiting the biological functions of said endogenous protein by enhancing the production of neutralizing antibodies against said protein by: ~~use of the method according to claim 23.~~

(i) Optionally, co-administering to a first mammal, at least one adenovirus and a nucleic acid sequence encoding said heterologous protein, said adenovirus being administered simultaneously, sequentially or separately with said nucleic acid sequence, and determining at least one amount of said heterologous protein and said adenovirus, sufficient to trigger an immune response against said heterologous protein by said first mammal; optionally, re-performing step (i) until said amount is determined;

(ii) co-administering to a second mammal a nucleic acid sequence encoding said heterologous protein, in an amount sufficient to trigger an immune response against said heterologous protein, as determined at step (i) and prior to or simultaneously adminstering said adenovirus, in an amount equal to or greater than the one determined at step (i) and sufficient to trigger an immune response against said adenovirus and sufficient to deplete or inhibit at least some antigen presenting cells of said mammal, and determining for said second mammal at least one amount of said adenovirus that reduces and/or suppresses the anti-heterologous protein immune response in said mammal; re-performing step (ii) until said amount is determined; and

wherein, (a) when one administers to a third mammal, said adenovirus in an amount equal or greater than the one determined at step (i) but lesser than the one determined at step (ii), said mammal produces neutralizing antibodies against said heterologous protein and optionally against said adenovirus; and (b) when one administers to said mammal said

adenovirus in an amount equal or greater than the one determined at step (ii), said mammal produces neutralizing antibodies against said adenovirus but produces no or few neutralizing antibodies against said heterologous protein.

30. (Currently Amended) ~~A~~ The method according to claim 29, wherein said disease is selected from the group consisting of auto-immune diseases, inflammatory diseases, cancers, viral infections, bacterial infections, parasitic infections, and fungal infections.

31-42. (Canceled)

43. (Currently Amended) ~~A~~ The method according to ~~any one of claims 1 to 26 and 33~~ claim 1, wherein said heterologous protein or a fragment thereof is selected from the group consisting of the proteins that are presented by class I major histocompatibility molecule (CMH I), a class II major histocompatibility molecule (CMH II), and a combination of a class I major histocompatibility molecule and a class II major histocompatibility molecule.

44. (Currently Amended) ~~A~~ The method according to claim 43, wherein said heterologous protein is selected from the group consisting of secreted proteins, membrane proteins, receptors, intracellular proteins, and nuclear proteins.

45. (Currently Amended) ~~A~~ The method according to claim 44, wherein said secreted protein is selected from the group consisting of neuromediators, hormones, interleukines, lymphokines, interferons, chemokines, and growth factors.

46. (Currently Amended) ~~A~~ The method according to ~~any one of claims 1 to 26 and 33~~ claim 1, wherein the mammal is selected from the group consisting of mouse, rat, rabbit, hamster, pig, cow, goat, sheep, horse, and primate.

47. (Currently Amended) ~~A~~ The method according to ~~any one of claims 1 to 26 and 33~~ claim 1, wherein the administration of said adenovirus and said ~~heterologous protein and/or~~ nucleic acid sequence encoding said heterologous protein is performed via a technique selected from the group consisting of intravenous injection, intravaginal injection, intrarectal injection, intramuscular injection, and intradermic injection.

48-71. (Canceled)

72. (Currently Amended) ~~A~~ The method according to ~~claim 64~~ claim 27, wherein an ~~additional~~ agent is further administered to said mammal in step (i) and (ii).

73. (Currently Amended) ~~A~~ The method according to ~~any one of claims 64 and 72~~ claim 27, wherein the amount of said adenovirus of step (ii) is at least twice the amount of said adenvirus determined at step (i).

74. (Currently Amended) ~~A~~ The method according to ~~claim 64~~ claim 27, wherein said mammal is a mouse and ~~said agent is a virus selected from the group consisting of adenovirus, adenovirus associated virus, retrovirus, pox virus, and vaccinia virus, and~~ wherein said ~~agent~~ adenovirus and said nucleic acid sequence encoding said heterologous protein are simulatenously co-administered as a recombinant ~~virus~~ adenovirus, the genome of which comprising at least said nucleic acid sequence encoding said heterologous protein.

75. (Currently Amended) ~~A~~ The method according to ~~claim 64~~ claim 27, wherein said mammal is a human and ~~said agent a virus selected from the group consisting of adenovirus, adenovirus associated virus, retrovirus, pox virus, and vaccinia virus, and~~ wherein said ~~agent~~ adenovirus and said nucleic acid sequence encoding said heterologous protein are simulatenously co-administered as a recombinant ~~virus~~ adenovirus, the genome of which comprising at least said nucleic acid sequence encoding said heterologous protein.

76. (Canceled)

77. (Currently Amended) ~~A~~ The method according to claim ~~76~~ 75 wherein the heterologous protein encoded by said recombinant adenovirus is a secreted protein.

78. (Currently Amended) ~~A~~ The method according to claim 77 wherein the nucleic acid sequence encodes the human thrombopoietin.

79. (Currently Amended) ~~A~~ The method according to claim 78 wherein the human thrombopoietin gene is under the control of the RSV promoter (AdRSVhuTPO).

80. (Currently Amended) A method of inhibiting in a mouse formation of neutralizing antibodies directed against ~~an~~ a heterologous protein, said method comprising:

(i) optionally, administering to a first mouse, a recombinant adenovirus, the genome of which comprising at least a nucleic acid sequence encoding said heterologous protein, and determining the amount of recombinant adenovirus particles that triggers an immune response towards said heterologous protein in said mouse without depleting or inhibiting at least some antigen presenting ~~cell~~ cells of said mouse, wherein:

(a) said amount of recombinant adenovirus particles is below ~~4.10^{10}~~ 4×10^{10} particles, and/or

(b) the amount of said adenovirus particles able to form plaque is below ~~4.10^{9}~~ 4×10^{9} pfu/mouse;

and optionally, re-performing step (i) until said amount is determined;

(ii) administering to a second mouse an amount of recombinant adenovirus particles in an amount greater that the one determined at step (i) and sufficient to trigger an immune response against said recombinant adenovirus particles and sufficient to deplete or inhibit at least some antigen presenting cells of said mouse, and determining for said second mouse at least one amount of said recombinant adenovirus particles that reduces and/or suppresses the anti-heterologous protein immune response in said mouse, wherein :

(a) said amount of recombinant adenovirus particles is at least equal to or greater than ~~4.10^{10}~~ 4×10^{10} particles, and/or

(b) the amount of said adenovirus particles able to form plaque is equal to or greater than ~~4.10^{9}~~ 4×10^{9} pfu/mouse;

and optionally re-performing step (ii) until said amount is determined;

wherein when one administers to said mouse said recombinant adenovirus particles in an amount equal or greater than the one determined at step (ii), said mouse produces neutralizing antibodies against said adenovirus but produces no or few neutralizing antibodies against said heterologous protein.

81. (Currently Amended) ~~A~~ The method according to claim 80, wherein an ~~additional~~ agent is further administered to said mouse in step (i) and (ii).

82. (Currently Amended) ~~A~~ The method according to ~~any one of claims 80-81~~ claim 80 or 81, wherein the amount of said recombinant adenovirus particles of step (ii) is at least twice the amount of said recombinant adenovirus particles determined at step

83. (Currently Amended) ~~A~~ The method according to claim 12, wherein said heterologous protein or a fragment thereof is selected from the group consisting of the proteins that are presented by class I major histocompatibility molecule (CMH I), a class II major histocompatibility molecule (CMH II), and a combination of a class I major histocompatibility molecule and a class II major histocompatibility molecule.

84. (Currently Amended) ~~A~~ The method according to claim 83, wherein said heterologous protein is selected from the group consisting of secreted proteins, membranes proteins, receptors, intracellular proteins, and nuclear proteins.

85. (Currently Amended) ~~A~~ The method according to claim 84, wherein said secreted protein is selected from the group consisting of neuromediators, hormones, interleukines, lymphokines, interferons, chemokines, and growth factors.

86. (Currently Amended) ~~A~~ The method according to claim 12, wherein the mammal is selected from the group consisting of mouse, rat, rabbit, hamster, cow, pig, goat, sheep, horse, and primate.

87. (Currently Amended) ~~A~~ The method according to claim 12, wherein the administration of said ~~agent~~ recombinant adenovirus and said nucleic acid sequence encoding said heterologous protein is performed via a technique chosen among intravenous injection, intravaginal injection, intrarectal injection, intramuscular injection, and intradermic injection.

88. (Currently Amended) ~~A~~ The method according to claim 87, wherein said intravenous injection is selected from the group consisting of retro-orbital sinus injection, tail injection, hepatic injection, femoral injection and jugular injection.